

Clinico-aetiological Profile of Neonatal Hypertension: An Observational Study

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ABSTRACT

Introduction: The incidence of hypertension among neonates admitted to the Neonatal Intensive Care Unit (NICU) is increasing. The reported incidence is between 0.2% and 3%. Blood Pressure (BP) among neonates varies considerably in the immediate postnatal period. The BP in neonates determined by birthweight, gestational age at birth and postnatal age. This variability in BP makes it challenging to diagnose neonatal hypertension. There is a paucity of Indian studies on neonatal hypertension. A systematic diagnostic evaluation of neonatal hypertension aids in early identification of the aetiology and further management.

Aim: To assess the incidence of hypertension in neonates in the NICU and to evaluate the aetiology and clinical profile of neonatal hypertension.

Materials and Methods: This was a hospital-based prospective observational study done at Sri Dharmasthala Manjunatheswara College of Medical Sciences and Hospital, Dharwad, Karnataka, India, between August 2016 and August 2021. A total of 29 neonates who had neonatal hypertension were included in the study after obtaining ethical committee clearance. All relevant data regarding demographic details, risk factors for hypertension, clinical features, probable aetiology, and relevant investigations were collected in a predesigned proforma. These neonates were followed-

up once a month until six months of age. All the data were entered in Microsoft Excel version 2203 and analysed using the Statistical Package for Social Sciences (SPSS) software version 20.0. The categorical variables were described as percentages. The numerical variables were compared using a Student's t-test and a Chi-square test. A p-value of 0.05 was considered statistically significant.

Results: In the present study, out of 13,345, a total of 29 (0.22%) neonates had hypertension. Hypertension was more prevalent among term (82.7%). Of the 29 neonates, 19 (65.5%) had an antenatal risk for hypertension. A total of 14 (48.3%) of neonates had an antenatally diagnosed renal and/or cardiac anomaly. The most common presentation of hypertension is asymptomatic. Thirteen (44.8%) neonates had transient hypertension, which resolved at the time of discharge, and 16 (55.2%) neonates had persistent hypertension, requiring antihypertensive medication and follow-up. The most common aetiology for hypertension was renal and renovascular causes (44.8%). Mortality in the present study was 10.3% (n=3).

Conclusion: Hypertension is an uncommon yet important problem in the NICU. In the majority of neonates, the presentation of hypertension is asymptomatic. Most common aetiology of hypertension being renal cause. Neonates with persistent hypertension may require long-term antihypertensive treatment and regular follow-up.

Keywords: Antihypertensive agent, Blood pressure, Clinical features, Newborn

INTRODUCTION

Hypertension in neonates is an important clinical problem that was first recognised in the 1970s [1]. There is an increased prevalence of hypertension in neonates admitted to the NICU [2]. With advances in neonatal care, the ability to identify, evaluate, and manage neonatal hypertension has improved.

Defining hypertension in the neonate is a challenging task. The BP of a neonate varies with the birth weight, gestational age, and postconceptional age. Intra-arterial monitoring is considered as gold standard method [3]. However, the oscillometric method is easy, non invasive, and able to follow BP trends over time. Studies have shown a reasonably good correlation between oscillometric and invasively measured BP in neonates [4]. Invasive BP monitoring is usually reserved for very sick neonates with haemodynamic instability.

A neonate is diagnosed to have hypertension, when there were three separate BP measurements with a systolic or mean reading greater than the 95th percentile for infants of similar gestational or postconceptional age and weight [5,6]. The oscillometric method is most commonly used method for BP measurement. The results of BP measurement by oscillometric measurement correlate with

those of the intra-arterial BP recordings [3]. Zubrow's chart [7] for the first week of age and thereafter, Dioene's BP percentile charts [8] were used for defining high BP readings [3].

Awareness about neonatal hypertension has increased in recent times. The reported incidence is between 0.2% and 3% [1,2,8,9]. The two most common causes of neonatal hypertension are renovascular and renal parenchymal disease [2,9]. Persistent hypertension during infancy and early childhood may be the primary cause of cardiovascular disease, chronic kidney disease, and stroke in adulthood [9].

There is very limited literature on the follow-up of these neonates with hypertension and its management. The present study was conducted to assess the incidence of hypertension in neonates admitted to the NICU and to evaluate the aetiology and clinical profile of neonatal hypertension and its management.

MATERIALS AND METHODS

The present study is a hospital-based prospective observational study conducted at Sri Dharmasthala Manjunatheswara College of Medical Sciences and Hospital, Dharwad, Karnataka, India. The

study was conducted for a period of five years, from August 2016 to August 2021. The study was conducted after obtaining Ethical Committee clearance (IEC letter number: SDMIEC/02021/15).

Inclusion criteria: Neonates admitted to the NICU with neonatal hypertension (BP greater than the 95th percentile for that particular gestational age and birth weight, measured on three separate occasions) were included in the study.

Exclusion criteria: The neonates, who were on ionotropic agents and neonates, who were diagnosed neonatal hypertension outside and on already on treatment referred to of hospital for further management were excluded from the study.

Sample size calculation: Sample size was calculated using the formula:

$$\text{Sample size, } n = \frac{Z (1-\alpha/2) \times P (1-P)}{d^2}$$

Here, prevalence= 2% [10] and d=0.05

n=30

So, 30 subjects were required for the study. The present study comprises of 29 participants.

Study Procedure

The measurement of BP was done using the oscillometric method with an appropriate BP cuff size as recommended by the 4th Task Force on Hypertension [6]. The Non Invasive Blood Pressure (NIBP) was recorded using a multiparameter patient monitor (Nihon Kohden Monitor, Dongguan Kangweile Electronic Technology Co., Ltd., Hong Kong).

In the present study, the BP measurement was done one hour after feeding and when the baby was asleep or quietly awake. Mean of three BP readings taken at least 30 minutes apart. BP greater than the 95th percentile for that particular gestational age and birth weight, measured on three separate occasions, is considered neonatal hypertension [10]. Zubrow's chart was diagnosed as hypertension for the first two weeks of life, and Dioene's BP percentiles, thereafter [7,8].

The neonates who were included in the present study were further classified into transient and persistent neonatal hypertension. The neonate who had hypertension readings initially, its usually after interventions (like treatment of underlying cause such as drugs, painful procedure and fluid overload) and who were normotensive and of antihypertensive agent at the time of discharge from the hospital were classified as transient hypertension. Otherwise, neonate who continues to have hypertension at time of discharge and required antihypertensive medicine for control of hypertension were classified as persistent hypertension [11].

Perinatal risk factors such as maternal medication, maternal hypertension, antenatal steroids, gestational diabetes, etc., were collected. Birth history such as mode of delivery, prolonged second stage, and Apgar score were noted [12,13]. During the NICU stay, details regarding any invasive procedure, such as the insertion of an umbilical vein and/or arterial catheter, surgery, and other procedures, were noted. The relevant blood, urine, and radiological investigations were done wherever required. Neonates with transient hypertension underlying cause for hypertension was been treated and neonates, who continue to have hypertension were treated with antihypertensive medication were medication.

Neonates with persistent hypertension continued to be followed-up once a month for six months [11]. During follow-up visits, the

general health state, BP, medications, and other relevant clinical details were noted. All relevant data were collected in a predesigned proforma after obtaining informed consent.

STATISTICAL ANALYSIS

All the data were entered in Microsoft Excel version 2203 and analysed using the SPSS software version 22.0 for Windows (IBM Corp., Armonk, NY, USA). The categorical variables were described as percentages. The numerical variables were compared using a Student's t-test and a Chi-square test. A p-value of 0.05 was considered statistically significant.

RESULTS

Out of 13,345 neonates admitted to NICU during study period, 60.7% (n=8,100) were males and remaining 39.3% (n=5,245) were females. Of these neonates 29 were found to have hypertension. This represents 0.22% (n=29) of all neonates admitted to NICU during the study period.

[Table/Fig-1] shows the demographic details of the neonates. The hypertension was more prevalent in neonate with term gestational age, male sex and normal birth weight, and this association was statistically significant. The mean systolic blood pressure at the time of diagnosis was 92.4 mmHg, mean diastolic blood pressure was 62.5 mmHg.

Demographic profile	Number (%)
Sex	
Male	19 (65.5)
Female	10 (34.4)
Gestational age (week)	
<28	0 (0)
28 to 31+6 days	2 (6.8)
32 to 34+6 days	2 (6.8)
34 to 36+6 days	1 (3.4)
>37	24 (82.7)
Birth weight (gram)	
<1000	1 (3.4)
1000 to 1500	2 (6.8)
1500 to 2500	5 (17.2)
>2500	21 (72.4)

[Table/Fig-1]: Demographic details of the neonates with hypertension. *p-value <0.05; (N=29)

In the present study, 65.5% (n=19), neonates had risk factors for the development of hypertension. The antenatal risk factors in present study being maternal hypertension, maternal medication (like steroid) and Gestational Diabetes Miletus (GDM). Antenatal risk factor for development of neonatal hypertension was found in 65.5% (n=19). A 27.6% (n=8) neonates had antenatally diagnosed renal and/or cardiac anomaly, most common congenital anomaly being renal. In present study, 6.9% (n=2) neonates presented with features of congestive cardiac failure secondary to hypertension and remaining 93.1% (n=27) neonates were asymptomatic, admitted to NICU for other cause and hypertension was an incidental finding.

In present study, aetiology of hypertension was established in 89.7% (n=26) cases and in 10.3% (n=3) cases cause for hypertension was not established, inspite of detailed investigation. The most common cause for hypertension being renal cause in 41.4% (n=12) cases [Table/Fig-2]. In the present study, of 29 neonates, 10 had Umbilical

Venous Catheter (UVC) inserted and Umbilical Artery Catheter (UAC) in one neonate. Of these 10 neonates, none of these neonates had any evidence of renal vein or artery thrombosis.

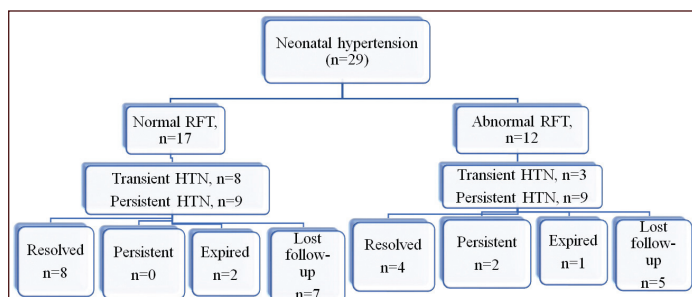
Aetiology	Number of cases (%) (N=29)
Renal cause (n=12) Obstructive uropathy	5 (17.2)
AKI	4 (13.8)
Polycystic kidney disease	2 (6.9)
Multicystic dysplastic kidney	1 (3.5)
Renovascular cause (n=2) Renal vein thrombosis	1 (3.5)
Renal artery stenosis	1 (3.5)
Respiratory cause (n=2) Bronchopulmonary dysplasia	1 (3.5)
Pneumothorax	1 (3.5)
Endocrine causes (n=2) Adrenal haemorrhage	1 (3.5)
Congenital adrenal hyperplasia	1 (3.5)
Cardiac cause (n=2) Coarctation of aorta	1 (3.5)
Severe aortic stenosis	1 (3.5)
Painful procedure (n=3) Like surgical intervention and mechanical ventilation	3 (10.3)
Medication (n=3) Like caffeine, steroids	3 (10.3)
No aetiology (n=3)	3 (10.3)

[Table/Fig-2]: Aetiology of neonatal hypertension.

AKI: Acute kidney injury

About 37% (n=11) neonates had transient hypertension. Transient was found secondary to drugs (caffeine, steroids etc.), painful invasive procedure (like surgery, mechanical ventilation, insertion of central venous catheter etc.), acute kidney injury and Intra-ventricular Haemorrhage (IVH). Transient hypertension resolved with the treatment of underlying cause and it lasted for about two weeks. A 62% (n=18) neonates had persistent hypertension during NICU stay and were discharged with oral antihypertensive medication. The antihypertensive used in these neonates are Amlodipine (n=1), Furosemide (n=5) and Enalapril (n=3). None of the neonate required {intravenous (i.v.)} antihypertensive agents.

In present study, out of 29 neonates, 41% (n=12) lost follow-up and 48.3% (n=14) babies who were regularly followed-up. Of these 14 neonates who were followed-up, 12 babies had resolution of hypertension by six month of age and two babies had persistent hypertension beyond six months of age and requiring long term oral antihypertensive medication. Mortality in our study was 10.3% (n=3), cause of death in all three neonates, was not related to hypertension [Table/Fig-3].



[Table/Fig-3]: Flowchart of neonates with hypertension included in the study and their follow-up.

RFT: Renal function test; HTN: Hypertension

DISCUSSION

The BP in neonates depends on a variety of factors. Hypertension can be seen in a variety of situations in NICU, prevalence of hypertension is more among sick neonate admitted to intensive care unit. In the present study, incidence of neonatal hypertension was 0.22%, which was in par with the most of studies [1,3,9], where incidence ranged from 0.2 to 0.3% [Table/Fig-4] [2,9,11,14,15].

Study	Study period	Place of study	Incidence
Adelman R [9]	February 1978 to January 1981	University of California School of Medicine Davis, California	0.2%
Singh HP et al., [14]	January 1983 to December 1988	Loyola University of Chicago, Maywood, Illinois.	0.81
Seliem WA et al., [2]	January 2001 to December 2005	Canberra Hospital, Australia	1.3%
Sahu R et al., [15]	January 2006 to December 2009	Children Memorial Hermann Hospital, Houston, Tx	1.3%
Skalina ME et al., [11]	January 1980 to December 1980	Rainbow Babies and Children Hospital, Cleveland, Ohio	2%
Present study	August 2016 to August 2021	SDM College of Medical Sciences and Hospital, India	0.22%

[Table/Fig-4]: Review of literature on incidence of neonatal hypertension [2,9,11,14,15].

There is an association between development of neonatal hypertension and UAC and/or UVC insertion. In the present study, 34.5% of neonates had umbilical line inserted had hypertension which correlates with the findings of the study done by Seliem WA et al., [2]. However, in the present study there was no association between UAC placement and development of thromboembolism. In the present study, one neonate had renal vein thrombosis as cause of neonatal hypertension but for that neonate UAC was not been inserted.

The present study supports the findings Seliem WA et al., that antenatal risk factors such as pregnancy induced hypertension and use of antenatal steroids were associated with development of neonatal hypertension [2]. Present study agrees with the results of Karen F et al., they concluded that most common cause was renal and renovascular lesions [16]. Seliem WA et al., and Rabe H et al., studied antenatal and postnatal risk factors for development of neonatal hypertension, found that neonatal hypertension is commonly associated with postnatal clinical problems [2,17]. In the present study, babies with underlying risk factors like renal/cardiac/endocrine disorder developed hypertension postnatally.

In the present study, 48.2% of cases are due to renal and renovascular aetiology, obstructive uropathy being the most common cause for neonatal hypertension. The present study results agrees with above study findings [Table/Fig-5] [11,14,16].

Study	Year	Number of cases	Renal cause
Skalina ME et al., [11]	1986	20	17 (85)
Buchi KF and Siegler RL [16]	1986	53	23 (43)
Singh HP et al., [14]	1992	26	13 (50)
Present study	2016	29	14 (48.2)

[Table/Fig-5]: Review of literature on common aetiology of Neonatal hypertension [11,14,16].

Study done by Seliem WA et al., 15% (n=3) of neonates, who had hypertension, at six months follow-up continued to have hypertension requiring long term antihypertensive treatment [2]. In present study, 6.8% (n=2) infants continues to have hypertension at six months, but in the present study 41.4% (n=12) neonates lost follow-up.

Limitation(s)

Invasive BP measurement could not be done in the present study. Long-term follow-up of all neonates was not done.

CONCLUSION(S)

Hypertension in neonate is an important yet not completely understood entity. With the better availability of data, understanding of neonatal hypertension continues to evolve. BP in neonates depends on a variety of factors such as birth weight, gestational age, antenatal risk factor, intervention done and underlying systemic condition. A careful diagnostic evaluation should lead to early determination of the underlying cause of hypertension in most infants and thus, aids in timely management. The transient hypertension resolves once, the underlying cause has been addressed. Persistent hypertension requires careful evaluation for underlying cause. Treatment decisions should be tailored based on severity of the hypertension and underlying aetiology. Further studies need on long-term follow-up and treatment.

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